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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,875	06/27/2005	Chris Armstrong	002.00240	6263

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EXAMINER	
HA, JULIE	
ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/510,875	ARMSTRONG ET AL.	
	Examiner	Art Unit	
	Julie Ha	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16 and 19-25* is/are pending in the application.

4a) Of the above claim(s) *19-23* is/are withdrawn from consideration.

5)☒ Claim(s) *10 and 11* is/are allowed.

6)☒ Claim(s) *1-6,8,9,12-16,24 and 25* is/are rejected.

7)☒ Claim(s) *7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment after Non-Final rejection filed on October 25, 2007 is acknowledged. Claims 17-18 have been cancelled. Claims 1-16 and 19-25 are pending in this application. Applicant elected without traverse Group I (claims 1-16, 24 and 25) in the reply filed on October 13, 2006. Restriction is deemed proper and is made FINAL. Claims 19-23 remain withdrawn from further consideration as being drawn to nonelected invention. Claims 1-16 and 24-25 are examined on the merits in this office action.

Julie Ha is the Examiner of record.

Withdrawn Objections

1. Objection to claims 1-9, 24 and 25 are hereby withdrawn due to Applicant's amendment to the claims.

2. Objection to claim 11 is hereby withdrawn due to Applicant's amendment to the claim.

Withdrawn Rejection

3. Claims 1-3, 6 and 8 rejected under 35 U.S.C. 102(a) is hereby withdrawn due to Applicant's arguments and amendment to the claims.

Maintained Rejection

35 U.S.C. 112, 1st

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-9, 12-16, 24 and 25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

6. Claims 1-6, 8, 9, 24 and 25 are drawn to a kit of parts comprising two or more protein kinase substrate polypeptides. Claims 8, 9, 24 and 25 also specify that the kit comprise a binding partner for the substrate peptides that is responsive to the phosphorylation state of the polypeptides. Claims 1-6, 12-16 are drawn to polypeptide comprising SEQ ID NO: 6 with up to 5 residues substituted and a consensus sequence. The specification discloses the complete structure of the following polypeptides comprising SEQ ID NO:6: RARTLSFAEPG, KKLNRTLSFAEPG and RRRLSFAEPG (recited in the legend for Figure 2). The claimed genus is much broader than this well-defined subgenus. The minimal structural requirements for the genus are that the

polypeptides comprise a phosphorylatable portion (i.e., a serine, threonine or tyrosine) and a specificity conferring portion that is different for each polypeptide in the kit. An infinite number of polypeptides could satisfy these minimal requirements. Despite this breadth, the specification does not disclose the complete or partial structure or chemical/physical properties of any additional peptides, or guidance on how to obtain specific polypeptides suitable for the kit. The consensus sequences recited in claim 15 are extremely broad. SEQ ID NOS: 2, 5, 8 and 9 have 4, 4, 4 and 5 undefined positions, respectively, with the only defined position in SEQ ID NO:2 being R in position 3 and S, and the only defined positions in SEQ ID NOS: 5, 8 and 9 being S. The specification provides no guidance on how to obtain a polypeptide that is capable of being bound by a binding partner where the binding partner is not specific for phosphotyrosine, phosphoserine or phosphothreonine, as recited in claim 1. Even if the kit includes antibodies specific for an epitope other than phosphotyrosine, phosphoserine or phosphothreonine, such antibodies would also bind to the substrate polypeptides of the kit. Likewise, the specification fails to fully describe the phosphorylation-state-sensitive binding partners for this genus of polypeptides. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

7. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for the purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117). The

specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). Therefore, only the polypeptides comprising SEQ ID NO: 6 (RARTLSFAEPG, KKLNRTLSFAEPG and RRRLSFAEPG recited in the legend for Figure 2), but not the full breadth of the claims, meet the written description provision of 35 U.S.C. § 112, first paragraph.

Response to Applicant's Arguments

8. Applicant argues that claim 1 has been amended to incorporate the limitation of claim 7, and "specification page 7, lines 19-23 indicates that the term LSFAEPG includes sequences with no, one, two, three, four or five residues (other than serine) conservatively substituted" (p. 27 of Applicant's Remark, 3rd paragraph). Furthermore, Applicant argues that "the inventors have surprisingly found that peptides that share a common epitope are phosphorylated efficiently by many different protein kinases, which fall into several kinase subfamilies. This was unexpected, because the prior art describes specific peptides as substrates for specific kinases, and a common epitope would not have been expected to have an appropriate conformation for phosphorylation by a range of protein kinases" (p. 27 of Applicant's Remark, 4th paragraph bridging p. 28). Applicant further argues that "the consensus sequences of SEQ ID NOS: 2, 5, 8 or 9 in claim 15 are adequately described. These consensus sequences are well known to those skilled in the art as being the sequences necessary for phosphorylation by the specified protein kinases" (p. 28 of Applicant's Remark, 2nd and 3rd paragraphs).

9. Applicant's arguments have been fully considered but have not been found persuasive because there are innumerable possibilities of substrate polypeptide of SEQ ID NO:6 having up to five residues conservatively substituted. Previous claim 7 was drawn to SEQ ID NO:6. The amended claim 1 is drawn to SEQ ID NO:6 having up to five residues conservatively substituted. Applicant describes that "by conservative substitutions is intended combinations such as Gly, Ala; Val, Ile, Leu; Asp, Glu; Asn, Gln; Ser, Thr; Lys, Arg; and Phe, Tyr" (see p. 8 of specification, lines 1-5). However, the "conservative substitutions" are not fully defined in the specification, since "combinations such as" means that there are other conservative substitutions available, and the listed are preferred embodiments. According to Protein Sequences in the CAS Registry File on STN, A, G, P, S and T are functionally similar; N, D, Q and E are functionally similar; R, H and K are functionally similar; I, M, L and V are functionally similar; F, W and Y are functionally similar. Therefore, SEQ ID NO:6 having the peptide sequence LSFAEPG can have multiple combinations of possibilities for up to 5 amino acid conservative substitution (excluding S). There are 7 amino acid residues, wherein 6 of them can be conservatively substituted. L can be substituted for I, M or V; F can be substituted for W or Y; A can be substituted for G, P, S or T; E can be substituted for N, D or Q; P can be substituted for A, G, S or T; G can be substituted for A, P, S or T. These are just the naturally occurring amino acids. There are non-natural amino acids, such as D-amino acids, β-amino acids, γ-amino acids, ε-amino acids, as well as amino acid mimetics and modified amino acids that have similar functionality. Therefore, there are vast numbers of polypeptides that could satisfy these minimal requirements.

Furthermore, there are variables that make the polypeptides much broader than the well-defined subgenus. For example, SEQ ID NO:2 is defined as: X_{aa1}-X_{aa2}-Arg-X_{aa4}-X_{aa5}-Ser, wherein X_{aa1} is R or K, X_{aa2} is any amino acid (20 naturally occurring and those non-natural amino acids), X_{aa4} is any amino acid (20 naturally occurring and those non-natural amino acids) and X_{aa5} is any amino acid (20 naturally occurring and those non-natural amino acids). Just having 3 amino acids that can be any amino acid, and only applying 20 naturally occurring amino acids, this implies that $3^{20}= 3.49 X10^{10}$ different possibilities for just the tripeptide (X_{aa2}, X_{aa4}, X_{aa5}). When non-natural amino acids and amino acid mimetics are considered, the numbers are infinite. Same logic flows for the SEQ ID NOS: 5, 8 and 9. Therefore, SEQ ID NOS: 2, 5, 8 and 9 are not fully and adequately described. Therefore, the rejection is maintained.

The following anticipation rejection is revised to include claims omitted in the first office action.

Rejection-35 U.S.C. 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-6, 8-9, 12, 14, 15 and 24-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Tan et al (WO 00/14536, cited on Information Disclosure Statement).

12. Tan et al teach libraries comprising more than two protein kinase substrate polypeptides each polypeptide comprising a specificity conferring portion which is different for each polypeptide and a phosphorylatable portion. The libraries include peptides with the sequences XXXXXXT*XXXXXXC (example I), PXS*P (example II), XXXXRSXS*XPXXXXC (example III), and PXT*/S*PXR (example IV), wherein X is any amino acid and * indicates phosphorylation. The T*, S* and T*/S* in these sequences represent the phosphorylatable portions whereas the flanking sequence represent the specificity conferring portion. Tan et al also teach antibodies that bind to these substrate peptides in a phosphorylation-dependent manner. The antibodies in example IV recognize the proline and arginines in addition to the phosphotyrosine and therefore are not simply anti-phosphotyrosine antibodies. Thus, the limitations of claims 1-4 are satisfied. With respect to claim 5, the library of example IV is conjugated to a tripeptide making it 9 amino acids in length. With respect to claim 6, the library of example IV is a substrate for a serine/threonine kinase. With respect to claims 8-9, 24 and 25, the antibody of example IV is reacted with the peptide library. With respect to claims 12, 14 and 15, Tan et al teaches a sequence (underlined portion of **XXXXRS**XS*XPXXXXC) having up to 5 amino acid residues of SEQ ID NO:6 conservatively substituted, and having a consensus sequence (SEQ ID NOS: 2 and 9) for a protein kinase that is to the N-terminus of SEQ ID NO: 6 (see example III). Since SEQ ID NO:2 comprises of

$X_{aa1}X_{aa2}RX_{aa4}X_{aa5}S$ wherein X_{aa1} is R or K, X_{aa2} is any amino acid, X_{aa4} is any amino acid and X_{aa5} is any amino acid, the consensus sequence having **XXXXRS** wherein X is any amino acid meets the limitation of SEQ ID NO:2. Furthermore, SEQ ID NO:9 comprises $X_{aa1}X_{aa2}X_{aa3}X_{aa4}X_{aa5}S$ wherein X_{aa1} is R or K, X_{aa2} is any amino acid, X_{aa3} is R or K, X_{aa4} is any amino acid and X_{aa5} is any amino acid, the consensus sequence having **XXXXRS** wherein X is any amino acid meets the limitation of SEQ ID NO:9. Additionally, both SEQ ID NOS: 5 and 8 are comprised of 5 residues, and SEQ ID NO:8 comprises $X_{aa1}X_{aa2}X_{aa3}X_{aa4}$Ser wherein X_{aa1} is R or K, X_{aa2} is R or K, X_{aa3} is R or K and X_{aa4} is any amino acid. Therefore, this meets the limitation of claims 12, 14 and 15. Although they are not called a kit by Tan et al, the library and antibody, the substrate peptide and binding partner are provided together.

Response to Applicant's Arguments

13. Applicant argues that "limitation of previous claim 7 has been incorporated into claim 1, and previous claim 7 was not rejected for anticipation by Tan". Applicant argues that claims 2-6, 8-9 and 24-25 depend from and further limit claim 1. Therefore, claims 2-6, 8-9, and 24-25 are novel over Tan for at least the same reasons that claim 1 is novel over Tan.

14. Applicant's arguments have been fully considered but have not been found persuasive because previous claim 7 was drawn to SEQ ID NO:6 (LSFAEPG), not to SEQ ID NO:6 having up to five residues conservatively substituted. Since there can be up to 5 residues conservatively substituted and Tan et al teach example III having the

sequence **XXXXRS**XS*XPXXXXC, and X is any amino acid and * indicates phosphorylation. Since Applicant has not defined what "conservative substitution" are and as described above, amino acid residues A, G, P, S and T are functionally similar; N, D, Q and E are functionally similar; R, H and K are functionally similar; I, M, L and V are functionally similar; F, W and Y are functionally similar, the underlined portion of the sequence can be "LS*FAEPG", where the 1st X is L, 2nd X is F, P can be conservatively substituted for A, 3rd X is E, 4th X is P and 5th X is G. The sequence N-terminal flanking to the LS*FAEPG sequence is the specificity conferring portion having the sequence **XXXXRS**, wherein X is any amino acid. Therefore, the Tan reference teaches all of the limitations of claims 1-6, 8-9, 12, 14-15 and 24-25. Therefore, the rejection is revised and maintained.

Conclusion

15. Claim 7 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

16. Claims 10 and 11 are allowable. Claims 1-6, 8-9, 12-16 and 24-25 have been rejected.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Julie Ha whose telephone number is 571-272-5982. The examiner can normally be reached on Mon-Fri, 8:00 am to 4:30 pm.

18. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

19. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Patent Examiner
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